Palladium-Catalyzed Carbonylation Reactions of Aryl Bromides at Atmospheric Pressure: A General System Based on Xantphos

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General Considerations. All reactions were carried out under an atmosphere of carbon monoxide. Carbon monoxide was purchased in a pressurized cylinder from Air Gas (C.P. grade, Part # CM CP200). Unless otherwise noted, THF, Et_2O, CH_2Cl_2 and toluene were purchased from J.T. Baker in CYCLE-TAINER® solvent-delivery kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina (for THF and Et_2O) or through neutral alumina and copper (II) oxide (for toluene and CH_2Cl_2).[1] Unless otherwise stated, commercially obtained materials were used without further purification. The following aryl bromides were purchased form Acros: 3-bromothiophene (filtered through basic alumina prior to use), 2-bromo-3-methylpyridine, 4-bromoisoquinoline and 3-bromoquinoline. The following aryl bromides were purchased from Lancaster: 3-bromonitrobenzene, 4-bromo-2-fluorobenzonitrile, methyl 3-bromobenzoate and 1-bromo-2-cyclohexylbenzene. The following aryl bromides were purchased from Alfa Aesar: 3-bromobenzonitrile (Avocado Organics), 4-chloro-bromobenzene (Avocado Organics), 3-chloro-bromobenzene (Avocado Organics), 4-bromoanisole (filtered through basic alumina prior to use), 1-bromonaphthalene (Avocado Organics), 2-bromobenzonitrile, 2-bromobenzotrifluoride (filtered through basic alumina prior to use), 4-bromo-dimethylaminoaniline (Avocado Organics), 2-bromopyridine (Avocado Organics), ethyl 3-bromobenzoate (Avocado Organics) and 2-bromoanisole (Avocado Organics; filtered through basic alumina prior to use). The following aryl bromides were purchased from Aldrich: 4-bromoveratrole (filtered through basic alumina prior to use), 4-bromobiphenyl, 2-(3-bromophenyl)-1,3-dioxolane (filtered through basic alumina prior to use), 2-bromo-*p*-xylene, methyl 2-bromobenzoate, 5-bromo-*m*-xylene, 4-bromobenzonitrile and 4-chlorobenzonitrile. The following compound was purchased from PCR Inc.: 2,5-difluorobromobenzene (filtered through basic alumina prior to use). *tert*-Butyl *N*-(4-bromophenyl)carbamate was prepared following literature procedures[2] using 4-bromoaniline (Aldrich), Di-*tert*-butyl dicarbonate (Aldrich) and Iodomethane (Alfa)**.** *N, O*-dimethylhydroxylamine hydrochloride was purchased from Aldrich and Alfa Aesar. All amines used in Table 3 were purchased from Aldrich with the exception of the following amines, which were purchased from Alfa Aesar: *N*-methyl piperazine, morpholine, and benzylamine. All amines were distilled from KOH under nitrogen. Triethyl amine was purchased from Aldrich and used as received without further purification. Xantphos, DPEphos, dppf, dppp, and dppb were purchased form Strem and used without further purification. SPhos was prepared according to the literature procedure[3] and (S)-BINAP was obtained as a gift from Rhodia. $Pd(OAc)_2$ was purchased from Strem, Inc. or supplied by BASF (formerly Englehard). Sodium Carbonate was purchased from Mallinckrodt. *Anhydrous tribasic potassium phosphate was purchased from Fluka Chemical Co. and used as supplied*. The source (and thus the particle size) of the base employed may be critical for achieving efficient reactions.

All products of Pd-catalyzed carbonylation reactions were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, as well as elemental analysis. Copies of ^{1}H and ^{13}C NMR spectra are included for compounds that failed to give satisfactory elemental analyses. All ^{1}H NMR experiments are reported in δ units, parts per million (ppm) downfield from tetramethylsilane (internal standard) and were measured relative to the signals for residual chloroform (7.26 ppm), methylene chloride (5.32 ppm), DMSO-d_6 (2.54 ppm) or benzene (7.16 ppm) in the deuterated solvents. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.23 ppm), deuteromethylene chloride (54.00 ppm), DMSO-d_6 (40.45 ppm) or deuterobenzene (128.39

ppm), and all were obtained with ^{1}H decoupling. All ^{31}P NMR spectra are reported in ppm relative to H_3PO_4 (0 ppm). All ^{19}F NMR spectra are reported in ppm relative to trichlorofluoromethane (0 ppm). Melting points are uncorrected. Gas Chromatographic analyses were performed using a FID detector using 25 m x 0.20 mm capillary column with cross-linked methyl siloxane as a stationary phase.

The conversions in Table 1 were determined by G.C. using dodecane as an internal standard, added during reaction workup. The yields in Table 1, entries 1 – 9 were also determined by G.C. using dodecane as an internal standard. The yield in Table 1, entry 10, is an isolated yield (average of two runs) and the procedure is given below. The yields in Tables 2, 3 and 4 are isolated yields (average of two runs). All compounds isolated were estimated to be ≥95% pure as determined by ^{1}H NMR and GC analysis and/or combustion analysis. The procedures described in this section are representative, and thus the yields may differ from those shown in Tables 1 - 4.

Note: carbon monoxide is a highly toxic gas and should only be used only in a well-ventilated fume hood and with proper leak detection equipment.

General Procedure A: Synthesis of Weinreb Amides via Pd-Catalyzed Aminocarbonylation. An oven-dried culture tube (18 x 150 mm, VWR) equipped with a Teflon® coated magnetic stir bar was sealed with a 14/20 rubber septum (inverted), evacuated, backfilled with nitrogen and cooled under nitrogen. All solid reagents were added by briefly removing the rubber septum: $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), and Na_2CO_3 (3 mmol, 3 equiv., 318 mg). Then, all liquid reagents were added dropwise via syringe: aryl bromide (1 mmol, 1 equiv.; aryl bromides which were solids at room temperature were added during the initial charge) and toluene (2 mL). After the addition of all reagents, the rubber septum was secured with several wrappings of electrical tape. Then, the reaction was purged for ~ 30 s with $CO_{(g)}$; following the gas purge a balloon was connected to the reaction using a short length of rubber tubing (~ 1 in.), a needle adapter and a 20 G needle. This balloon was then inflated with $CO_{(g)}$ and the reaction tube was submerged in a 80 ºC preheated oil bath. The reaction mixture was heated at 80 °C with vigorous stirring until the aryl halide had been completely consumed as judged by GC analysis. The reaction mixture was then allowed to cool to room temperature, diluted with ethyl acetate (~ 10 mL), filtered through a plug of celite (eluting with ethyl acetate) and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel.

General Procedure B: Synthesis of Weinreb Amides via Pd-Catalyzed Aminocarbonylation of *ortho*-Substituted Aryl Halides. An oven-dried culture tube (18 x 150 mm, VWR) equipped with a Teflon® coated magnetic stir bar was sealed with a 14/20 rubber septum (inverted), evacuated, backfilled with nitrogen and cooled under nitrogen. All solid reagents were added by briefly removing the rubber septum: $Pd(OAc)_2$ (2.5 mol %, 0.025 mmol, 0.025 equiv., 5.6 mg), Xantphos (5 mol %, 0.05 mmol, 0.05 equiv., 28.9 mg), *N, O*-dimethylhydroxylamine

hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), and K_3PO_4 (3 mmol, 3 equiv., 637 mg). Then, all liquid reagents were added dropwise via syringe: aryl bromide (1 mmol, 1 equiv.; aryl bromides which were solids at room temperature were added during the initial charge) and solvent (2 mL, toluene or *m*-xylene). After the addition of all reagents, the rubber septum was secured with several wrappings of electrical tape. Then, the reaction was purged for ~ 30 s with $CO_{(g)}$; following the gas purge a balloon was connected to the reaction using a short length of rubber tubing (~ 1 in.), a needle adapter and a 20 G needle. This balloon was then inflated with $CO_{(g)}$ and the reaction tube was submerged in a 100 - 120 ºC preheated oil bath. The reaction mixture was heated at 100 - 120 °C with vigorous stirring until the aryl halide had been completely consumed as judged by GC analysis. The reaction mixture was then allowed to cool to room temperature, diluted with ethyl acetate (~ 10 mL), filtered through a plug of celite (eluting with ethyl acetate) and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel.

General Procedure C: Pd-Catalyzed Aminocarbonylation of Functionalized Aryl Bromides. A screw-capped test tube (*NOT* OVEN DRIED) equipped with a Teflon-coated stir bas was capped with a Teflon-lined septum and charged with all solid reagents: $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), Xantphos (11.6 mg, 0.02 mmol), aryl bromide (if solid, 1.0 mmol), and Na_2CO_3 (159 mg, 1.5 mmol) or Et_3N (210 μL, 1.5 mmol). All further manipulations were carried out in a well-ventilated hood. The tube was then evacuated, backfilled with carbon monoxide and a balloon was connected to the reaction (using a short length of rubber tubing, ~ 1 in., a needle adapter and a 20 G needle) and inflated with carbon monoxide. Then all liquid reagents were added via syringe: aryl bromide (if liquid, 1.0 mmol), amine (1.5 mmol), and dry toluene (1 mL). If NEt_3 was used as the base it was added (210 mL, 1.5 mmol) after the amine. The reaction vessel was then submerged in a preheated oil bath at 80 °C and stirred for 15 h (reaction times not optimized). After this time, the reaction mixture was allowed to cool to room temperature. Ethyl acetate (2-3 mL), and dodecane (100 μL, GC standard) were added and the crude reaction mixture was analyzed by GC. The reaction mixture was purified by flash column chromatography on silica gel to afford the desired product.

General Procedure D: Synthesis of Esters via Pd-Catalyzed Carbonylation. A culture tube (18 x 150 mm, VWR; *NOT* OVEN DRIED) equipped with a Teflon® coated magnetic stir bar was sealed with a 14/20 rubber septum (inverted), evacuated, backfilled with nitrogen and cooled under nitrogen. All solid reagents were added by briefly removing the rubber septum: $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg). Then, all liquid reagents were added via syringe: aryl bromide (1 mmol, 1 equiv.; aryl bromides which were solids at room temperature were added during the initial charge), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL). After the addition of all reagents, the rubber septum was secured with several wrappings of electrical tape. Then, the reaction was purged for ~ 30 s with $CO_{(g)}$; following the gas purge a balloon was connected to the reaction using a short length of rubber tubing (~ 1 in.), a needle adapter and a 20 G needle, This balloon was then inflated with $CO_{(g)}$ and the reaction tube was submerged in a 70 ºC preheated oil bath. The reaction mixture was stirred at 70 °C for 24 h. The reaction mixture was then allowed to cool to room temperature, diluted with ethyl acetate (~ 10 mL), filtered through a plug of celite (eluting with ethyl acetate) and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel.

3-Cyano-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 1).[4] Following general procedure A, a mixture of 3-bromobenzonitrile (1mmol, 0.182 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 8 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a viscous light orange oil (181 mg, 95 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04-8.01 (m, 1H), 7.97-7.93 (dm, *J* for the d = 7.98 Hz, 1H), 7.78-7.73 (dm, *J* for the d = 7.70 Hz, 1H), 7.55 (ddd, *J* = 0.55, 7.70, 7.98 Hz, 1H), 3.54 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.1, 135.0, 133.7, 132.5, 131.8, 128.9, 118.0, 112.1, 61.2, 33.1. IR (neat, cm^{-1}): 3075, 2975, 2938, 2821, 2232, 1647,1602, 1578, 1486, 1460, 1436, 1412, 1384, 1178, 986, 799, 734, 684. Anal. Calcd for $C_{10}H_9FN_2O_2$: C, 57.69; H, 4.36. Found: C, 57.64; H, 4.37.

4-Cyano-3-fluoro-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 2).[4] Following general procedure A, a mixture of 4-bromo-2-fluorobenzonitrile (1mmol, 0.200 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 18 h. The crude product mixture was purified by flash column chromatography on silica gel (20 % - 50 % ethyl acetate in hexanes) to provide the title compound as a light yellow-orange solid (181 mg, 95 %), mp 43 - 44 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.71-7.66 (m, 1H), 7.60-7.52 (m, 2H), 3.54 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.4, 164.2, 160.8, 140.8, 140.7, 133.4, 124.7, 124.7, 116.6, 116.4, 113.4, 103.3, 103.1, 61.6, 33.2 (observed complexity due to C-F splitting; definitive assignments have not yet been made). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -106.1**.** IR (neat, cm^{-1}): 3090, 2977, 2940, 2823, 2239, 1652, 1622, 1566, 1503, 1459, 1428, 1386, 1251, 1198, 1182, 1115, 990, 941, 887, 835, 750, 733, 714, 682, 668.

3-Nitro-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 3).[4] Following general procedure A, a mixture of 3-bromonitrobenzene (1mmol, 0.202 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 8 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a tan colored solid (185 mg, 88 %), mp 41 – 43 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.60-8.58 (t, *J* = 19 Hz, 1H), 8.35-8.31 (ddd, *J* = 1.1, 2.5, 8.2 Hz, 1H), 8.07-8.03 (dt, *J* = 1.4, 7.7 Hz, 1H), 7.65-7.59 (t, *J* = 8 Hz, 1H), 3.57 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.0, 147.6, 135.4, 134.3, 129.2, 125.2, 123.4, 61.3, 33.1. IR (neat, cm^{-1}): 3087, 2974, 2938, 2822, 1648, 1616, 1577, 1532, 1485, 1459, 1438, 1417, 1383, 1351, 1215, 1170, 1099, 983, 918, 858, 815, 715.

Thiophene-3-*N*-methoxy-*N*-methyl carboxamide (Table 2, entry 4).[4] Following general procedure A, a mixture of 3-bromothiophene (1mmol, 0.163 g, 94 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 21 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a very light yellow oil (155 mg, 90

%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09-8.06 (dd, *J* = 1.1, 3.0 Hz, 1H), 7.59-7.57 (dd, *J* = 1.1, 5.1, 1H), 7.31-7.27 (dd, *J* = 3.0, 5.2 Hz, 1H), 3.66 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.6, 134.4, 130.8, 129.0, 124.8, 61.1, 33.2. IR (neat, cm^{-1}): 3109, 2970, 2936, 2819, 1627, 1518, 1458, 1427, 1387, 1350, 1217, 1182, 1153, 1078, 985, 931, 881, 851, 816, 792, 733, 707, 667, 621.

4-Chloro-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 5).[4] Following general procedure A, a mixture of 4-chloro-bromobenzene (1mmol, 0.191 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 19 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (173 mg, 87 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.79-7.64 (m, 2H), 7.41-7.36 (m, 2H), 3.54 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.5, 136.6, 132.3, 129.8, 128.2, 61.1, 33.4. IR (neat, cm^{-1}): 3067, 2970, 2935, 2818, 1917, 1643, 1594, 1567, 1490, 1460, 1416, 1380, 1275, 1213, 1176, 1148, 1111, 1091, 1016, 995, 979, 887, 840, 746, 691, 656, 627.

***tert*-Butyl *N*-methyl-*N*-(4- *N*-methoxy-*N*-methyl-benzamide)carbamate (Table 2, entry 6).**[4] Following general procedure A, a mixture of *tert*-Butyl *N*-(4-bromophenyl)carbamate (1mmol, 0.285 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 13 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a light brown oil (210 mg, 95 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.73-7.66 (m, 2H), 7.33-7.28 (m, 2H), 3.57 (s, 3H), 3.37 (s, 3H), 3.29 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.0, 154.2, 145.7, 130.1, 128.7, 124.2, 80.6, 60.9, 36.8, 33.6, 28.1, 27.7. IR (neat, cm^{-1}): 2976, 2934, 2819, 1791, 1703, 1644, 1607, 1569, 1512, 1477, 1456, 1422, 1367, 1315, 1300, 1279, 1254, 1216, 1153, 1109, 1065, 1018, 995, 977, 889, 851, 807, 770, 758, 734, 700.

4-*N*-Dimethoxy-*N*-methyl-benzamide (Table 2, entry 7).[4] Following general procedure A, a mixture of 4-bromoanisole (1mmol, 0.187 g, 125 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 8 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (210 mg, 95 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.77-7.70 (m, 2H), 6.94-6.88 (m, 2H), 3.85 (s, 3H), 3.57 (s, 3H), 3.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.2, 161.4, 130.4, 125.8, 113.1, 60.7, 55.2, 33.7. IR (neat, cm^{-1}): 3074, 3002, 2966, 2936, 2840, 2559, 2048, 1639, 1608, 1575, 1512, 1462, 1421, 1375, 1304, 1255, 1216, 1173, 1112, 1064, 1029, 994, 977, 888, 842, 796, 756, 703, 676, 631, 593.

***N*-Methoxy-*N*-methyl-isophthalamic acid methyl ester (Table 2, entry 8).**[4] Following general procedure A, a mixture of methyl 3-bromobenzoate (1mmol, 0.215 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-

dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), Na_2CO_3 (3 mmol, 3 equiv., 318 mg), and toluene (2 mL) was heated at 80 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (196 mg, 88 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.38-8.33 (t, *J* = 1.7 Hz, 1H), 8.17-8.10 (ddd, *J* = 1.4, 1.7, 7.9 Hz, 1H), 7.91-7.84 (ddd, *J* = 1.4, 1.7, 7.7 Hz, 1H), 7.54-7.46 (dt, *J* = 1.7, 7.7 Hz, 1H), 3.94 (s, 3H), 3.56 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.7, 166.2, 134.3, 132.41, 131.37, 129.9, 129.2, 128.1, 61.0, 52.1, 33.3. IR (neat, cm^{-1}): 3072, 2953, 1725, 1645, 1582, 1487, 1435, 1381, 1300, 1278, 1208, 1170, 1109, 1085, 991, 972, 922, 824, 772, 724, 665, 633, 575.

3-[1,3]Dioxolan-2-yl-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 9).[4] Following general procedure A (a screw-capped test tube with a Teflon-lined septum was used in place of the culture tube and rubber septum), a mixture of 2-(3-bromophenyl)-1,3-dioxolane (1mmol, 151 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), triethylamine (3 mmol, 3 equiv., 420 μL), and toluene (1 mL) was heated at 80 ºC for 15 h. The crude product mixture was purified by flash column chromatography on silica gel (67 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (220 mg, 93 %). ^{1}H NMR (400 MHz, $CDCl_3$) 7.78 (s, 1 H), 7.67 (d, 1 H, *J* = 7.5 Hz), 7.56 (d, 1 H, *J* = 7.5 Hz), 7.41 (dd, 1 H, *J* = 7.5 Hz), 5.83 (s, 1 H), 4.00-4.14 (m, 4 H), 3.53 (s, 3 H), 3.33 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.4, 138.0, 134.1, 128.8, 128.6, 128.0, 126.3, 103.1, 65.2, 60.9, 33.6. IR ($CDCl_3$, cm^{-1}) 2972, 2937, 2892, 1639.

3,4,*N*-Trimethoxy-*N*-methyl-benzamide (Table 2, entry 10).[4] Following general procedure A (a screw-capped test tube with a Teflon-lined septum was used in place of the culture tube and rubber septum), a mixture of 4-bromoveratrole (1mmol, 144 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), triethylamine (3 mmol, 3 equiv., 420 μL), and toluene (1 mL) was heated at 80 ºC for 15 h. The crude product mixture was purified by flash column chromatography on silica gel (67 % ethyl acetate in hexanes) to provide the title compound as a colorless solid (202 mg, 90 %), mp 55 – 57 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) 7.39 (dd, 1 H, *J* = 2 Hz, 8 Hz), 7.32 (d, 1 H, *J* = 2 Hz), 6.87 (d, 1 H, *J* = 8 Hz), 3.92 (s, 3 H), 3.91 (s, 3 H), 3.58 (s, 3 H), 3.36 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) □ 168.9, 150.8, 148.0, 125.9, 121.8, 111.7, 109.9, 60.7, 55.7, 55.6, 33.7. IR ($CDCl_3$, cm^{-1}) 2966, 2937, 1631, 1517. m. p. 56 - 57 °C. Anal. Cald. for $C_{11}H_{15}NO_4$; C: 58.66, H: 6.71; Found C: 58.61, H: 6.77.

Biphenyl-4- *N*-methoxy-*N*-methyl carboxamide (Table 2, entry 11).[4] Following general procedure A (a screw-capped test tube with a Teflon-lined septum was used in place of the culture tube and rubber septum), a mixture of 4-bromobiphenyl (1mmol, 0.233 g), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg), Xantphos (2 mol %, 0.02 mmol, 0.02 equiv., 11.6 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), triethylamine (3 mmol, 3 equiv., 420 μL), and toluene (1 mL) was heated at 80 ºC for 15 h. The crude product mixture was purified by flash column chromatography on silica gel (40 % ethyl acetate in hexanes) to provide the title compound as a colorless solid (226 mg, 94 %), mp 80 – 82 ºC, lit. mp 77 – 78 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) 7.77-7.81 (m, 2 H), 7.61-7.67 (m, 4 H), 7.37-7.50

(m, 3 H), 3.61 (s, 3 H), 3.40 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 143.2, 140.0, 132.7, 128.8, 128.7, 127.8, 127.1, 126.6, 61.0, 33.7. IR ($CDCl_3$, cm^{-1}) 2971, 2936, 1632.

***N*-Methoxy-2,5,*N*-trimethyl-benzamide (Table 2, entry 12).**[4] Following general procedure B, a mixture of 2-bromo-*p*-xylene (1mmol, 0.185 g, 138 μL), $Pd(OAc)_2$ (2.5 mol %, 0.025 mmol, 0.025 equiv., 5.6 mg), Xantphos (5 mol %, 0.05 mmol, 0.05 equiv., 28.9 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and toluene (2 mL) was heated at 100 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide a mixture of rotamers (ratio not determined) of the title compound as a colorless oil (166 mg, 86 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.12-7.06 (m, 3H), 3.56 (brs, 3H), 3.31 (brs, 3H), 2.32 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.8, 134.5, 133.9, 130.6, 129.2, 129.2, 129.0, 125.8, 59.9, 31.9, 19.8, 17.7. IR (neat, cm^{-1}): 3018, 2969, 2932, 2818, 2736, 1903, 1844, 1651, 1612, 1577, 1502, 1459, 1422, 1375, 1287, 1242, 1181, 1157, 1126, 1062, 1041, 998, 980, 922, 887, 838, 816, 777, 746, 706, 694, 642, 597.

Naphthalene-1- *N*-methoxy-*N*-methyl carboxamide (Table 2, entry 13).[4] Following general procedure B, a mixture of 1-bromonaphthalene (1mmol, 0.207 g, 139 μL), $Pd(OAc)_2$ (2.5 mol %, 0.025 mmol, 0.025 equiv., 5.6 mg), Xantphos (5 mol %, 0.05 mmol, 0.05 equiv., 28.9 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and toluene (2 mL) was heated at 100 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide a mixture of rotamers (ratio not determined) of the title compound as a light orange oil (208 mg, 97 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.94-7.85 (m, 3H), 7.58-7.47 (m, 4H), 3.4 (brs, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.1, 132.7, 129.1, 128.9, 127.8, 126.3, 125.3, 124.3, 124.2, 123.7, 60.5, 32.4. IR (neat, cm^{-1}): 3280, 3056, 3005, 2971, 2935, 2817, 1947, 1820, 1651, 1592, 1580, 1508, 1474, 1439, 1422, 1374, 1266, 11232, 1183, 1167, 1102, 1027, 1014, 975, 891, 865, 801, 779, 740, 697, 647, 629, 580.

2-Cyano-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 14).[4] Following general procedure B, a mixture of 2-bromobenzonitrile (1mmol, 0.182 g), $Pd(OAc)_2$ (2.5 mol %, 0.025 mmol, 0.025 equiv., 5.6 mg), Xantphos (5 mol %, 0.05 mmol, 0.05 equiv., 28.9 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and toluene (2 mL) was heated at 100 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide a mixture of rotamers (ratio not determined) the title compound as a colorless oil (161 mg, 84 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.74-7.70 (ddd, J = 0.55, 1.38, 7.7 Hz, 1H), 7.69-7.50 (m, 3H), 3.52 (brs, 3H), 3.40 (brs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.5, 138.2, 132.4, 132.3, 129.7, 127.3, 116.6, 109.9, 61.0, 32.3. IR (neat, cm^{-1}): 3292, 3071, 2976, 2938, 2822, 2229, 1657, 1595, 1572, 1492, 1459, 1445, 1421, 1385, 1289, 1219, 1191, 1168, 1117, 1062, 1036, 982, 891, 772, 759, 720, 687, 634.

***N*-Methoxy-*N*-methyl-phthalamic acid methyl ester (Table 2, entry 15).**[4] Following general procedure B, a mixture of methyl 2-bromobenzoate (1mmol, 0.215 g, 140 μL), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3

equiv., 637 mg), and toluene (2 mL) was heated at 100 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (20 - 50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (186 mg, 83 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04-7.97 (d, *J* = 7.7 Hz, 1H), 7.63-7.55 (dt, *J* = 1.4, 7.4 Hz, 1H), 7.52-7.45 (dt, *J* = 1.4, 7.7 Hz, 1H), 7.45-7.38 (d, *J* = 7.4 Hz), 3.91 (s, 3H), 3.74 (brs, 3H), 3.35 (brs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 172.0, 166.1, 137.2, 132.3, 129.7, 128.9, 127.7, 126.9, 60.9, 52.4, 33.1. IR (neat, cm^{-1}): 3067, 2953, 2939, 2904, 2820, 2845, 1726, 1662, 1599, 1578, 1492, 1459, 1413, 1435, 1379, 1280, 1211, 1192, 1166, 1130, 1091, 1062, 1040, 991, 964, 883, 828, 802, 777, 739, 723, 703, 667, 631, 576.

2,*N*-Dimethoxy-*N*-methyl-benzamide (Table 2, entry 16).[4] Following general procedure B, a mixture of 2-bromoanisole (1mmol, 0.187 g, 125 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and toluene (2 mL) was heated at 100 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide a mixture of rotamers (ratio not determined) of the title compound as a colorless plates (174 mg, 89 %), mp 47 – 49 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40-7.32 (ddd, *J* = 1.6, 7.4, 8.2 Hz, 1H), 7.30-7.24 (dd, *J* = 1.4, 7.4 Hz, 1H), 7.01-6.95 (dt, *J* = 0.8, 7.4 Hz, 1H), 6.95-6.90 (d, *J* = 8.3 Hz, 1H), 3.84 (s, 3H), 3.49 (brs, 3H), 3.33 (brs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.8, 155.2, 130.1, 126.9, 124.7, 119.9, 110.6, 60.4, 55.1, 31.6. IR (neat, cm^{-1}): 3067, 3003, 2970, 2938, 2939, 1651, 1601, 1584, 1495, 1465, 1437, 1418, 1381, 1284, 1249, 1209, 1182, 1164, 1116, 1064, 1045, 1022, 987, 940, 884, 795, 758, 697, 630.

2-Trifluoromethyl-*N*-Methoxy-*N*-methy-benzamide (Table 2, entry 17).[4] Following general procedure B, a mixture of 2-bromobenzotrifluoride (1mmol, 0.225 g, 136 μL, filtered through basic alumina prior to use), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and *m*-xylene (2 mL) was heated at 110 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (20 - 50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil and a 1.1:1 mixture of rotamers (214 mg, 92 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.75-7.67 (d, J = 7.4 Hz, 1H), 7.65-7.50 (m, 2H), 7.46-7.40 (m, 1H), 3.89 (brs, 0.6H), 3.42 (s, 2.4H), 3.37 (s, 2.3H), 3.05 (brs, 0.7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.1, 164.4, 133.7, 132.1, 131.3, 129.5, 128.9, 127.2, 126.8, 126.2, 1259, 125.3, 121.6, 118.0, 60.4, 59.7, 36.1, 31.9 (observed complexity due to C-F splitting; definitive assignments have not yet been made). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -60.2**.** IR (neat, cm^{-1}): 3071, 2977, 2941, 2823, 1667, 1606, 1584, 1503, 1426, 1445, 1416, 1384, 1317, 1272, 1213, 1171, 1130, 1077, 1049, 1034, 991, 961, 891, 879, 772, 742, 708, 655, 632.

3-Methyl-pyridine-2-*N*-methoxy-*N*-methyl carboxamide (Table 2, entry 18).[4] Following general procedure B, a mixture of 2-bromo-3-methylpyridine (1mmol, 0.172 g, 111 μL), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and *m*-xylene (2 mL) was heated at 110 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 - 60 % ethyl acetate in hexanes) to provide the title compound as a light yellow oil and a 1:1 mixture of

rotamers (140 mg, 77 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.44-8.36 (dd, J = 0.8, 4.7 Hz, 1H), 7.60-7.48 (d, J = 7.1 Hz, 1H), 7.27-7.16 (dd, J = 4.9, 7.7 Hz, 1H), 3.89 (brs, 0.6H), 3.52 (s, 2.4H), 3.37 (s, 2.4H), 3.13 (brs, 0.6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.8, 153.3, 145.7, 137.5, 129.8, 123.4, 61.1, 31.4, 17.1. IR (neat, cm^{-1}): 3055, 2977, 2938, 2821, 1655, 1575, 1485, 1446, 1407, 1384, 1274, 1260, 1238, 1186, 1169, 1119, 1072, 983, 896, 889, 818, 800, 743, 692, 639, 580.

2-Cyclohexyl-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 19).[4] Following general procedure B, a mixture of 1-bromo-2-cyclohexylbenzene (1mmol, 0.239 g), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and *m*-xylene (2 mL) was heated at 120 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (30 - 50 % ethyl acetate in hexanes) to provide a mixture of rotamers (ratio not determined) of the title compound as a viscous colorless oil (213 mg, 86 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.41-7.30 (m, 2H), 7.24-7.14 (m, 2H), 3.85 (brs, 1H), 3.38 (brs, 5H), 2.75 (brs, 1H), 1.60-1.95 (m, 5H), 1.2-1.58 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.1, 143.9, 134.2, 128.7, 125.6, 125.4, 124.8, 60.2, 41.0, 33.6, 31.6, 26.3, 25.5. IR (neat, cm^{-1}): 3292, 3061, 3025, 2926, 2851, 2817, 2668, 1651, 1599, 1575, 1489, 1448, 1410, 1378, 1264, 1218, 1193, 1168, 1140, 1117, 1093, 1060, 1044, 989, 893, 884, 863, 829, 771, 755, 705, 644, 634, 625, 577, 530.

2,5-Difluoro-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 20).[4] Following general procedure B, a mixture of 2,5-difluorobromobenzene (1mmol, 0.193 g, filtered through basic alumina prior to use), $Pd(OAc)_2$ (2.5 mol %, 0.025 mmol, 0.025 equiv., 5.6 mg), Xantphos (5 mol %, 0.05 mmol, 0.05 equiv., 28.9 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and *m*-xylene (2 mL) was heated at 110 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (140 mg, 70 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.19-7.03 (m, 3H), 3.56 (brs, 3H), 3.36 (brs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.7, 159.7, 156.4, 156.1, 152.9, 124.7, 124.6, 124.4, 124.3, 117.9, 117.6, 117.1, 117.0, 116.8, 116.7, 115.4, 115.1, 61.1, 31.9 (observed complexity due to C-F splitting; definitive assignments have not yet been made). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -118.8, -120.4**.** IR (neat, cm^{-1}): 3074, 2977, 2940, 2823, 1659, 1599, 1495, 1437, 1405, 1383, 1266, 1251, 1205, 1149, 1104, 1059, 992, 939, 879, 851, 822, 786, 735, 706, 690, 640, 604.

4-Cyano-*N*-methoxy-*N*-methyl-benzamide (Table 2, entry 21).[4] Following general procedure B, a mixture of 4-chlorobenzonitrile (1mmol, 0.146 g), $Pd(OAc)_2$ (3.0 mol %, 0.03 mmol, 0.03 equiv., 6.7 mg), Xantphos (6 mol %, 0.06 mmol, 0.06 equiv., 34.7 mg), *N, O*-dimethylhydroxylamine hydrochloride (1.5 mmol, 1.5 equiv., 146 mg), K_3PO_4 (3 mmol, 3 equiv., 637 mg), and toluene (2 mL) was heated at 105 ºC for 20 h. The crude product mixture was purified by flash column chromatography on silica gel (50 % ethyl acetate in hexanes) to provide the title compound as a colorless oil (149 mg, 78 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.81-7.64 (m, 4H), 3.53 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.7, 138.2, 131.7, 128.6, 118.0, 113.8, 61.2, 33.0. IR (neat, cm^{-1}): 3093, 3066, 2974, 2938, 2821, 2230, 1937, 1651, 1609, 1560, 1507, 1461, 1422, 1383, 1286, 1215, 1180, 1149, 1115, 1065, 1020, 980, 889, 851, 7777,

754, 703, 668, 638, 575. Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30. Found: C, 63.12; H, 5.33.

4-Cyano-*N*-(4-methoxy-benzyl)-benzamide (Table 3, entry 1).[5] Using general procedure C with NEt_3 as the base at 60 °C, 4-bromo-benzonitrile (182 mg, 1.0 mmol), 4-methoxy-benzylamine (196 μL, 1.5 mmol), 60 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (6:4) as the eluent to afford the title product as a yelloworange solid (223 mg, 84 % yield). R_f = 0.27 (hexane/ethyl acetate = 6:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.83 (d, 2 H, *J* = 11 Hz), 7.58 (d, 2 H, *J* = 11 Hz), 7.18 (d, 2 H, *J* = 11 Hz), 6.79 (d, 2 H, *J* = 11 Hz), 4.45 (d, 2 H, *J* = 11 Hz), 3.74 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.7, 159.1, 138.3, 132.2, 129.8, 129.2, 127.9, 118.1, 114.8, 114.1, 55.3, 43.7. IR ($CDCl_3$, cm^{-1}) 3339, 3054, 2987, 1664, 1514. m. p.133 - 134 °C.

***N*-Benzyl-3,5-dimethyl-benzamide (Table 3, entry 2).**[6] Using general procedure C with Na_2CO_3 as the base, 5-bromo-*m*-xylene (135 mL, 1.0 mmol), *N*-benzylamine (164 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a colorless solid (235 mg, 98 % yield). R_f = 0.36 (hexane/ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.04 (s, 2 H), 7.28-7.39 (m, 5 H), 7.14 (s, 1 H), 6.41 (brs, 1 H), 4.65 (d, 2 H, *J* = 5.5 Hz), 2.35 (s, 6 H).

3,5-Dimethyl-*N*-(3-phenyl-propyl)-benzamide (Table 3, entry 3). Using general procedure C with NEt_3 as the base, 5-bromo-*m*-xylene (135 mL, 1.0 mmol), 3-phenyl-propylamine (213 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (8:2) as the eluent to afford the title product as a colorless oil (244 mg, 91% yield). R_f = 0.14 (hexane/ethyl acetate = 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.50 (m, 8 H), 6.30 (brs, 1 H), 3.66 (dt, 2 H, *J* = 6 Hz, 7.5 Hz), 2.89 (t, 2 H, *J* = 7.5 Hz), 2.50 (s, 6 H), 2.13 (q, 2 H, *J* = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 141.6, 137.9, 134.6, 132.7, 128.3, 128.2, 125.8, 124.7, 39.7, 33.4, 31.0, 21.1. IR ($CDCl_3$, cm^{-1}) 3327, 3029, 2925, 1645, 1602, 1523. A satisfactory elemental analysis was not obtained for this compound: Anal. Cald. for $C_{18}H_{21}NO$; C: 80.86, H: 7.92; Found C: 79.89, H: 7.89. **The ^{1}H and ^{13}C NMR spectra follow**.

(3,5-Dimethyl-phenyl)-morpholin-4-yl-methanone (Table 3, entry 4).[7] Using general procedure C with Na_2CO_3 as the base and with less catalyst, 0.5 mol% (1.25 mg) $Pd(OAc)_2$, 0.5 mol % (2.9 mg) Xantphos, 5-bromo-*m*-xylene (135 mL, 1.0 mmol), morpholine (131 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as a colorless oil (205 mg, 93 % yield). R_f = 0.36 (hexane/ethyl acetate = 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.05 (s, 1 H), 7.00 (s, 2 H), 3.22-4.04 (brm, 8 H), 2.33 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.5, 138.0, 135.2, 131.1, 124.4, 66.7, 48.0 (br), 42.3 (br), 21.0. IR ($CDCl_3$, cm^{-1}) 2970, 2922, 2861, 1625, 1601.

(4-Methoxy-phenyl)-morpholin-4-yl-methanone (Table 3, entry 5).[8] Using general procedure C with Na_2CO_3 as the base, 3-bromo-anisole (125 mL, 1.0 mmol), morpholine (131 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as a colorless oil (230

mg, 87 % yield). R_f = 0.22 (hexane/ethyl acetate = 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.37 (d, 2 H, *J* = 11.5 Hz), 6.90 (d, 2 H, *J* = 11.5 Hz), 3.82 (s, 3 H), 3.50-3.78 (brm, 8 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.1, 160.6, 129.0, 127.0, 113.5, 66.6, 55.1, 47.9, 42.9. IR ($CDCl_3$, cm^{-1}) 2967, 2924, 2860, 1614.

(4-Dimethylamino-phenyl)-(4-methyl-piperazin-1-yl)-methanone (Table 3, entry 6).[9] Using general procedure C with NEt_3 as a base, (4-Bromo-phenyl)-dimethyl-amine (200 mg, 1.0 mmol), *N*-methylpiperazine (166 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using dichloromethane (saturated with NH_4OH)/methanol (10:1) as the eluent to afford the title product as a slightly yellow oil (228 mg, 92 % yield). R_f = 0.48 (CH_2Cl_2/methanol = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (d, 2 H, *J* = 8.5), 6.66 (d, 2 H, *J* = 8.5), 3.70 (s, 4 H), 2.99 (s, 6 H), 2.41 (brs, 4 H), 2.31 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.7, 151.1, 128.9, 121.9, 110.7. IR ($CDCl_3$, cm^{-1}) 2943, 2859, 2801, 1610.

3-(Piperidine-1-carbonyl)-benzoic acid methyl ester (Table 3, entry 7). Using general procedure C with Na_2CO_3 as the base, 3-bromochlorobenzene (117 mL, 1.0 mmol), piperidine (145 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as an orange oil (208 mg, 84 % yield). R_f = 0.44 (hexane/ethyl acetate = 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10-8.04 (m, 2 H), 7.56-7.62 (m, 1 H), 7.45-7.52 (m, 1 H), 3.92 (s, 1 H), 3.71 (brs, 2 H), 3.32 (brs, 2 H), 1.68 (brs, 4 H), 1.52 (brs, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.9, 166.1, 136.6, 131.1, 130.2, 130.1, 128.5, 127.7, 52.1, 48.6, 42.9, 26.3, 25.4, 24.3. IR ($CDCl_3$, cm^{-1}) 3002, 2944, 2860, 1721, 1623. A satisfactory elemental analysis was not obtained for this compound: Anal. Cald. for $C_{14}H_{17}NO_3$; C: 68.00, H: 6.93; Found C: 66.46, H: 6.91. **The ^{1}H and ^{13}C NMR spectra follow**.

3-Chloro-*N*-phenyl-benzamide (Table 3, entry 8).[10] Using general procedure C with Na_2CO_3 as the base, 3-chloro-bromobenzene (117 mL, 1.0 mmol), aniline (100 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (9:1) as the eluent to afford the title product as a colorless solid (237 mg, 99 % yield). R_f = 0.15 (hexane/ethyl acetate = 9:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.36 (s, 1 H), 8.02 (t, 1 H, *J* = 2 Hz), 7.90-7.94 (m, 1 H), 7.64-7.68 (m, 1 H), 7.76-7.81 (m, 2 H), 7.56 (t, 1 H, *J* = 7.6 Hz), 7.33-7.40 (m, 2 H), 7.09-7.15 (m, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 164.1, 138.9, 136.9, 133.2, 131.3, 130.4, 128.7, 127.4, 126.5, 123.9, 120.4. IR ($CDCl_3$, cm^{-1}) 3447, 3252, 3069, 1668, 1544.

4-Cyano-*N*-methyl-*N*-phenyl-benzamide (Table 3, entry 9).[11] Using general procedure C with NEt_3 as a base, 4-bromo-benzonitrile (182 mg, 1.0 mmol), *N*-methylaniline (163 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a slightly yellow solid (221 mg, 94 % yield). R_f = 0.16 (hexane/ethyl acetate = 7:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44-7.51 (m, 2 H), 7.35-7.42 (m, 2 H), 7.16-7.30 (m, 3 H), 6.98-7.05 (m, 2 H), 3.51 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.4, 143.7, 140.2, 131.5, 129.3, 129.0, 127.0, 126.8, 118.0, 112.8, 38.1. IR ($CDCl_3$, cm^{-1}) 3067, 2940, 1643, 1596.

***N*,*N*-Dibutyl-4-methoxy-benzamide (Table 3, entry 10).**[12] Using general procedure C with Na_2CO_3 as the base, 4-bromo-anisole (125 mL, 1.0 mmol), di-*n*-butylamine (164 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a colorless oil (230 mg, 87 % yield). R_f = 0.26 (hexane/ethyl acetate = 7:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.24 (d, 2 H, J = 9 Hz), 6.80 (d, 2 H, J = 9 Hz), 3.71 (brs, 3 H), 3.04-3.51 (brm, 4 H), 0.60-1.70 (brm, 14 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 160.1, 129.5, 128.3, 113.5, 48.9, 44.5, 30.8, 29.6, 20.2, 13.8. IR ($CDCl_3$, cm^{-1}) 2961, 2934, 2675, 1611.

(2,5-Dimethyl-phenyl)-morpholin-4-yl-methanone (Table 3, entry 11). Using general procedure C with Na_2CO_3 as the base at 100 °C, 1-bromo-2,4-dimethylbenzene (138 mL, 1.0 mmol), morpholine (131 μL, 1.5 mmol), 100 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as a colorless oil (199 mg, 85 % yield). R_f = 0.34 (hexane/ethyl acetate = 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.08 (s, 1 H), 6.96 (s, 2 H), 3.72-3.89 (m, 4 H), 3.52-3.62 (m, 2 H), 3.20-3.22 (m, 2 H), 2.30 (s, 3 H), 2.25 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.0, 135.4, 135.4, 130.7, 130.2, 129.6, 126.1, 66.8, 66.7, 47.0, 41.7, 20.7, 18.4. IR ($CDCl_3$, cm^{-1}) 2971, 2923, 2860, 1626. A satisfactory elemental analysis was not obtained for this compound: Anal. Cald. for $C_{13}H_{17}NO_2$; C: 71.21, H: 7.81; Found C: 70.76, H: 7.91. **The ^{1}H and ^{13}C NMR spectra follow**.

***N*-Hexyl-2,5-dimethyl-benzamide (Table 3, entry 12).** Using general procedure C with Na_2CO_3 as the base at 100 °C, 1-bromo-2,4-dimethylbenzene (138 mL, 1.0 mmol), morpholine (131 μL, 1.5 mmol), 100 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as a colorless solid (199 mg, 85 % yield). R_f = 0.34 (hexane/ethyl acetate = 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.14 (s, 1 H), 7.09 (s, 2 H), 5.76 (brs, 1 H), 3.37-3.45 (m, 2 H), 2.38 (s, 3 H), 2.31 (s, 3 H), 1.54-1.64 (m, 2 H), 1.28-1.42 (m, 6 H), 0.90 (t, 3 H, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.4, 136.8, 135.4, 132.7, 131.0, 130.5, 127.4, 39.9, 31.6, 29.8, 26.8, 22.7, 21.0, 19.4, 14.2. IR ($CDCl_3$, cm^{-1}) 3441, 3293, 2859, 1640, 1521. m. p. 84 - 85 °C. Anal. Cald. for $C_{15}H_{23}NO$; C: 77.21, H: 9.93; Found C: 77.35, H: 10.05.

***N*-Benzyl-2-methoxy-benzamide (Table 3, entry 13).** Using general procedure C with Na_2CO_3 as the base at 100 °C, 2-bromo-anisole (125 mL, 1.0 mmol), benzylamine (164 μL, 1.5 mmol), 100 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a colorless solid (226 mg, 94 % yield). R_f = 0.20 (hexane/ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (dd, 1 H, J = 2, 8 Hz), 8.22 (brs, 1 H), 7.43-7.50 (m, 1 H), 7.28-7.41 (m, 5 H), 7.07-7.14 (m, 1 H), 6.98 (d, 1 H, J = 8 Hz), 4.71 (d, 2 H, J = 5.5 Hz), 3.93 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.3, 157.4, 138.7, 132.7, 132.1, 128.5, 127.3, 127.0, 121.2, 121.1, 111.3, 55.8, 43.5. IR ($CDCl_3$, cm^{-1}) 3403, 3031, 2944, 1650, 1535. m. p. 85 - 86 °C. Anal. Cald. for $C_{15}H_{15}NO_2$; C: 74.67, H: 6.27; Found C: 74.54, H: 6.15.

Naphthalene-1-carboxylic acid benzylamide (Table 3, entry 14).[13,14] Using general procedure C with Na_2CO_3 as the base, 1-bromo-naphthalene (139 mL, 1.0 mmol), *N*-benzylamine (164 μL,

1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a colorless solid (247 mg, 95 % yield). R_f = 0.30 (hexane/ethyl acetate = 7:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.31-8.40 (m, 1 H), 7.84-7.96 (m, 2 H), 7.28-7.67 (m, 9 H), 6.34 (brs, 1 H), 4.73 (d, 2 H, *J* = 6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.5, 138.3, 134.2, 133.6, 130.6, 130.2, 128.7, 128.3, 127.8, 127.5, 127.1, 126.4, 125.5, 125.0, 124.7, 43.9. IR ($CDCl_3$, cm^{-1}) 3437, 3066, 1654, 1517.

***N*-Benzyl-phthalimide (Table 3, entry 15).** Using general procedure C with Na_2CO_3 as the base, 2-Bromo-benzoic acid methyl ester (140 mL, 1.0 mmol), *N*-benzylamine (164 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a white solid (201 mg, 85 % yield). R_f = 0.43 (hexane/ethyl acetate = 7:3). Commercially available from Aldrich.

***N*-(3-Phenyl-propyl)-phthalimide (Table 3, entry 16).**[15] Using general procedure C with Na_2CO_3 as the base, 2-Bromo-benzoic acid methyl ester (140 mL, 1.0 mmol), 3-Phenyl-propylamine (213 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a yellow solid (225 mg, 85 % yield). R_f = 0.43 (hexane/ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80-7.85 (m, 2 H), 7.67-7.75 (m, 2 H), 7.11-7.29 (m, 5 H), 3.75 (t, 2 H, J = 7 Hz), 2.69 (t, 2 H, J = 8 Hz), 1.98-2.09 (m, 2 H).

***N*-Benzyl-5-fluoro-phthalimide (Table 3, entry 17).** Using general procedure C with Na_2CO_3 as the base, methyl 2-bromo-4-fluorobenzoate (233 mg, 1.0 mmol), *N*-benzylamine (164 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as the eluent to afford the title product as a yellow solid (215 mg, 84 % yield). R_f = 0.39 (hexane/ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83-7.87 (m, 1 H), 7.51-7.54 (m, 1 H), 7.42-7.45 (m, 2 H), 7.26-7.41 (m, 4 H), 4.85 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 166.8, 166.5, 165.0, 136.0, 134.9, 134.8, 128.6, 128.5, 127.8, 125.6, 120.9, 120.7, 111.2, 110.9, 41.7. IR ($CDCl_3$, cm^{-1}) 1776, 1715, 1616, 1393. A satisfactory elemental analysis was not obtained for this compound: Anal. Cald. for $C_{15}H_{10}FNO_2$; C: 70.58, H: 3.95; Found C: 70.02, H: 3.89. **The ^{1}H and ^{13}C NMR spectra follow**.

2-(Morpholine-4-carbonyl)-benzoic acid methyl ester (Table 3, entry 18). Using general procedure C with Na_2CO_3 as the base, (140 mL, 1.0 mmol), morpholine (131 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:4) as the eluent to afford the title product as a colorless solid (191 mg, 77 % yield). R_f = 0.17 (hexane/ethyl acetate = 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (dd, 1 H, *J* = 1 Hz, 4 Hz), 7.59 (ddd, 1 H, *J* = 1 Hz, 4 Hz), 7.47 (ddd, 1 H, *J* = 1 Hz, 4 Hz), 7.30 (dd, 1 H, *J* = 1 Hz, 4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.6, 165.7, 138.0, 132.8, 130.4, 128.7, 127.1, 126.6, 66.3, 66.1, 52.3, 47.0, 41.8. IR ($CDCl_3$, cm^{-1}) 2925, 2955, 2861, 1725, 1635. m. p. 129 - 130 °C. Anal. Cald. for $C_{13}H_{15}NO_4$; C: 62.64, H: 6.07; Found C: 62.63, H: 6.09.

***N*,*N*-Dibutyl-nicotinamide (Table 3, entry 19).**[16] Using general procedure C with NEt_3 as a base, 3-bromo-pyridine (98 mL, 1.0 mmol), di-*n*-butylamine (164 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl

acetate (1:4) as the eluent to afford the title product as a yellow oil (182 mg, 78 % yield). R_f = 0.21 (hexane/ethyl acetate = 1:4). ^{1}H (400 MHz, $CDCl_3$) δ: 8.41-8.45 (m, 2 H), 7.48-7.53 (m, 1 H), 7.12-7.17 (m, 1 H), 3.30 (t, 2 H, *J* = 7.5 Hz), 3.00 (t, 2 H, *J* = 7.5 Hz), 1.39-1.52 (m, 2 H), 1.25-1.37 (m, 2 H), 1.14-1.25 (m, 2 H), 0.89-1.00 (m, 2 H), 0.77 (t, 3 H, *J* = 7.5 Hz), 0.59 (t, 3 H, *J* = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.7, 150.0, 147.2, 134.2, 133.0, 123.2, 48.7, 44.6, 30.7, 29.4, 20.1, 19.5, 13.8, 13.4. IR ($CDCl_3$, cm^{-1}) 2961, 2934, 2875, 1624.

Quinoline-3-carboxy-*N*-methyl-*N*-phenyl-amide (Table 3, entry 20). Using general procedure C with NEt_3 as a base and dioxane (1mL) as solvent, 3-bromo-quinoline (125 mL, 1.0 mmol), *N*-methylaniline (163 μL, 1.5 mmol), 80 °C, 15 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) as the eluent to afford the title product as a colorless solid (233 mg, 89 % yield). R_f = 0.27 (hexane/ethyl acetate = 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.72 (d, 1 H, *J* = 2 Hz), 8.20 (d, 1 H, *J* = 2 Hz), 7.96-8.03 (m, 1 H), 7.67-7.76 (m, 2 H), 7.48-7.56 (m, 1 H), 7.07-7.29 (m, 5 H), 3.58 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.7, 149.3, 147.5, 143.9, 136.9, 130.5, 129.3, 128.9, 128.7, 128.2, 126.9, 126.8, 126.8, 126.5, 38.2. IR ($CDCl_3$, cm^{-1}) 3067, 2940, 1636, 1595. m. p. 107 - 108 °C. A satisfactory elemental analysis was not obtained for this compound: Anal. Cald. for $C_{17}H_{14}N_2O$; C: 77.84, H: 5.38; Found C: 77.42, H: 5.34. **The ^{1}H and ^{13}C NMR spectra follow**.

Methyl 4-methoxybenzoate (Table 4, entry 1).[17] Following general procedure D, a mixture of 4-bromoanisole (1mmol, 125 μL), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (gradient: 0% to 10 % ethyl acetate in hexanes) to provide the title compound as an off-white solid (149 mg, 90 %), mp 48 – 49 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.02 - 7.92 (m, 2H), 6.98 - 6.86 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.91, 163.39, 131.65, 122.62, 113.66, 55.45, 51.92. IR (neat, cm^{-1}): 3003, 2955, 2843, 1713, 1609, 1579, 1512, 1435, 1320, 1286, 1261, 1170, 1106, 1027, 968, 911, 848, 771, 733, 698, 648, 633, 613, 514. Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.02; H, 6.12.

Methyl 3-cyanobenzoate (Table 4, entry 2).[17] Following general procedure D, a mixture of 3-bromobenzonitrile (1mmol, 182 mg), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (gradient: 0% to 10 % ethyl acetate in hexanes) to provide the title compound as a viscous light orange oil (148 mg, 92 %), mp 61 - 62 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.35 – 8.32 (m, 1H), 8.30 – 8.25 (m, 1H), 7.88 – 7.82 (m, 1H), 7.64 – 7.56 (m, 1H), 3.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.9, 135.9, 133.6, 133.1, 131.3, 129.5, 117.8, 112.8, 52.6. IR (neat, cm^{-1}): 2229, 1717, 1683, 1653, 1601, 1578, 1559, 1578, 1559, 1540, 1507, 1446, 1422, 1315, 1289, 1201, 1178, 1106, 1088, 1002, 988, 919, 865, 825, 751, 678, 569, 494. Anal. Calcd for $C_9H_7NO_2$: C, 67.07; H, 4.38. Found: C, 66.67; H, 4.48.

1-Ethyl 3-methyl benzene-1,3-dicarbonate (Table 4, entry 3). Following general procedure D, a mixture of ethyl 3-bromobenzoate (1mmol, 160 μL), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02

equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (gradient: 0 % to 10 % ethyl acetate in hexanes) to provide the title compound as a colorless viscous oil (196 mg, 94 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.69 - 8.66 (m, 1H), 8.26 -8.19 (m, 2H), 7.56 - 7.49 (m, 1H), 4.41 (q, *J* = 7.15 Hz, 2H), 3.94 (s, 3H), 1.41 (t, *J* = 7.15 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.3, 165.7, 133.8, 133.7, 130.9, 130.6, 130.5, 128.6, 61.4, 52.4, 14.4. IR (neat, cm^{-1}): 3078, 2984, 2954, 2907, 1725, 1610, 1587, 1434, 1393, 1368, 1308, 1244, 1193, 1166, 1133, 1096, 1077, 1023, 979, 934, 887, 863, 825, 785, 729, 676, 655. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.60; H, 5.81.

Methyl 4-(*tert*-butoxycarbonyl(methyl)amino)benzoate (Table 4, entry 4). Following general procedure D, a mixture of *tert*-butyl *N*-(4-bromophenyl)carbamate (1mmol, 265 mg), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (gradient: 0 % to 20 % ethyl acetate in hexanes) to provide the title compound as a colorless viscous oil (230 mg, 86 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.06 – 7.92 (m, 2H), 7.37 – 7.28 (m, 2H), 3.89 (s, 3H), 3.29 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.4, 153.9, 147.8, 129.9, 126.2, 124.2, 80.9, 51.9, 36.7, 28.2. IR (neat, cm^{-1}): 2977, 1928, 1703, 1606, 1575, 1512, 1478, 1435, 1392, 1349, 1282, 1155, 1113, 1017, 975, 860, 833, 801, 775, 705, 671, 635, 615, 572, 503. Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22. Found: C, 63.69; H, 7.42.

Methyl 4-cyano-3-fluorobenzoate (Table 4, entry 5). Following general procedure D, a mixture of 4-bromo-2-fluorobenzonitrile (1mmol, 200 mg), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product mixture was purified by flash column chromatography on silica gel (gradient: 0 % to 20 % ethyl acetate in hexanes) to provide the title compound as an off-white solid (177 mg, 99 %), mp 68 - 69 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.98 - 7.92 (dd, *J* = 8.06, 1.46 Hz, 1H), 7.90 - 7.86 (dd, *J* = 9.25, 1.47 Hz), 7.78 - 7.71 (dd, *J* = 8.06, 6.14 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.5, 164.2, 161.0, 136.5, 136.4, 133.7, 125.6, 125.6, 117.4, 117.1, 113.1, 105.4, 105.2, 117.4, 117.1, 113.1, 105.4, 105.2, 52.9. (observed complexity due to C-F splitting; definitive assignments have not yet been made). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -105.7**.** IR (neat, cm^{-1}): 3081, 2962, 2239, 1730, 1572, 1498, 1420, 1284, 1224, 1122, 1087, 985, 918, 903, 844, 800, 760, 733, 713, 524, 498, 447. A satisfactory elemental analysis was not obtained for this compound: Anal. Calcd for $C_9H_6FNO_2$: C, 60.34; H, 3.38. Found: C, 61.03; H, 3.61. The ^{1}H, ^{13}C and ^{19}F NMR spectra follow.

Methyl isoquinoline-4-carboxylate (Table 4, entry 6). Following general procedure D, a mixture of 4-bromoisoquinoline (1mmol, 208 mg), $Pd(OAc)_2$ (2 mol %, 0.02 mmol, 0.02 equiv., 4.5 mg) and Xantphos (4 mol %, 0.04 mmol, 0.04 equiv., 23.1 mg), methanol (10 mmol, 10 equiv., 405 μL), and triethylamine (2 mL) was heated at 70 ºC for 24 h. The crude product

mixture was purified by flash column chromatography on silica gel (gradient: 0 % to 25 % to 40 % ethyl acetate in hexanes) to provide the title compound as an off-white or tan solid (171 mg, 91 %), mp 77 - 80 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.36 (s, 1H), 9.18 (s, 1H), 8.98 - 8.89 (brd, *J* = 8.7 Hz, 1H), 8.6 - 7.98 (brd, *J* = 8.15 Hz, 1H), 7.88 - 7.78 (m, 1H), 7.72 - 7.62 (m, 1H), 4.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 156.8, 146.7, 133.6, 132.0, 128.2, 128.0, 127.5, 124.8, 120.1, 52.2. IR (neat, cm^{-1}): 3098, 3013, 2958, 1723, 1667, 1624, 1571, 1503, 1460, 1436, 1415, 1392, 1377, 1294, 1258, 1237, 1209, 1169, 1144, 1113, 1044, 1022, 976, 953, 917, 864, 796, 761, 748, 667, 629, 509. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85. Found: C, 70.27; H, 4.83.

Xantphospalladiumbenzoyl bromide (1a): $Pd_2(dba)_3$ (0.62 g, 0.68 mmol) and xantphos (0.79 g, 1.36 mmol) were charged to an oven-dried Schlenk flask equipped with a magnetic stirbar. The flask was sealed with a rubber septum and the contents placed under N_2. Degassed, dry toluene[1,18] (20 mL) was added to the flask via syringe, resulting in a dark-purple solution. The flask placed in a dry-ice acetone bath and the solution was stirred for 10 mins. Benzyl bromide (0.33 g, 1.77 mmol, 0.21 mL) was added via syringe to the cold solution and the resulting solution was stirred for 15 mins. The flask was removed from the cooling bath and the solution was warmed to rt, where it was stirred for 1 h. The resulting green grey solution was filtered under nitrogen (filter cannula) to remove trace palladium-black and the supernate was concentrated in vacuo to a volume of ca. 5 mL. Degassed, dry ether (20 mL) was added via syringe and the resulting single-phase solution was allowed to stand overnight resulting in the formation of an orange solid. The supernate was decanted (syringe) and the product was washed with degassed, dry ether (2 X 10 mL) under nitrogen. The product was dried in vacuo, then transferred into a nitrogen-filled glovebox. The crude product was then recrystallized (THF/pentane), filtered and dried in vacuo to provide 780 mg (61%) of xantphospalladiumbenzoyl bromide as a moisture-sensitive, orange micro-cystalline solid as the mono-THF, 1/6th n-pentane solvate. X-ray quality crystals were obtained by slow diffusion of pentane into a THF solution of **1a**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.73 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.34–7.42 (m, 8H), 7.22–7.34 (m, 5H), 7.17 (t, *J* = 7.2 Hz, 8H), 7.08–7.14 (m, 4H), 6.82-6.88 (m, 2H), 1.69 (s, 6H); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 3.96; IR (CH_2Cl_2 solution, cm^{-1}) cm 3055, 2987,1665,1423. A satisfactory elemental analysis was not obtained for this compound: Anal. Calcd for $C_{46}H_{37}BrO_2P_2Pd$•THF•1/6(C_5H_{12}): C, 63.99; H, 4.96. Found: C, 63.47; H, 4.84. The ^{13}C spectrum was complex due to ^{31}P splitting and was not tabulated (see below). **The ^{1}H, ^{13}C and ^{31}P NMR spectra follow.**

Pd-Catalyzed Aminocarbonylation using 1a:

In a nitrogen-filled glovebox, a culture tube (18 x 150 mm, VWR, not oven dried) equipped with a Teflon® coated magnetic stir bar was charged with **1a** (18.8 mg, 20 μmol, 2 mol%) and then sealed with an inverted 14/20 rubber septum. This setup was removed from the glove box and Na_2CO_3 (159 mg, 1.5 equiv, 1.5 mmol) was added in air by briefly removing the rubber septum. The septum was returned to the tube and secured with electrical tape. The tube was evacuated and backfilled with CO (balloon). A stock solution (2 mL) containing 5-bromo-meta-xylene (0.5 M, 1 mmol, 1.0 equiv), benzyl amine (0.6 M, 1.2 mmol, 1.2 equiv) and dodecane (0.13 M, 0.25 mmol, 0.25 equiv) in toluene was added via syringe. The reaction mixture was heated at 80 °C with vigorous stirring for 7 min. The reaction mixture was quickly cooled to rt in a water bath and diluted with EtOAc (6 mL). A sample was filtered through a plug of Celite and analyzed by GC. Conversion of the 5-bromo-meta-xylene was 25%, yield of the

amide was 26%. Repeating the above experiment and stopping the reaction at 40 min, showed 99% conversion of the starting material and 102% (GC) yield of the amide. These experiments establish the kinetic and chemical competency of **1a** as a catalyst for the aminocarbonylation reaction.

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(18) Toluene was further sparged with N_2 for 20 min prior to use in this experiment.

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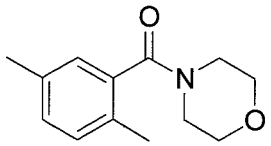

Table 3, Entry 11

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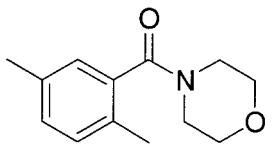

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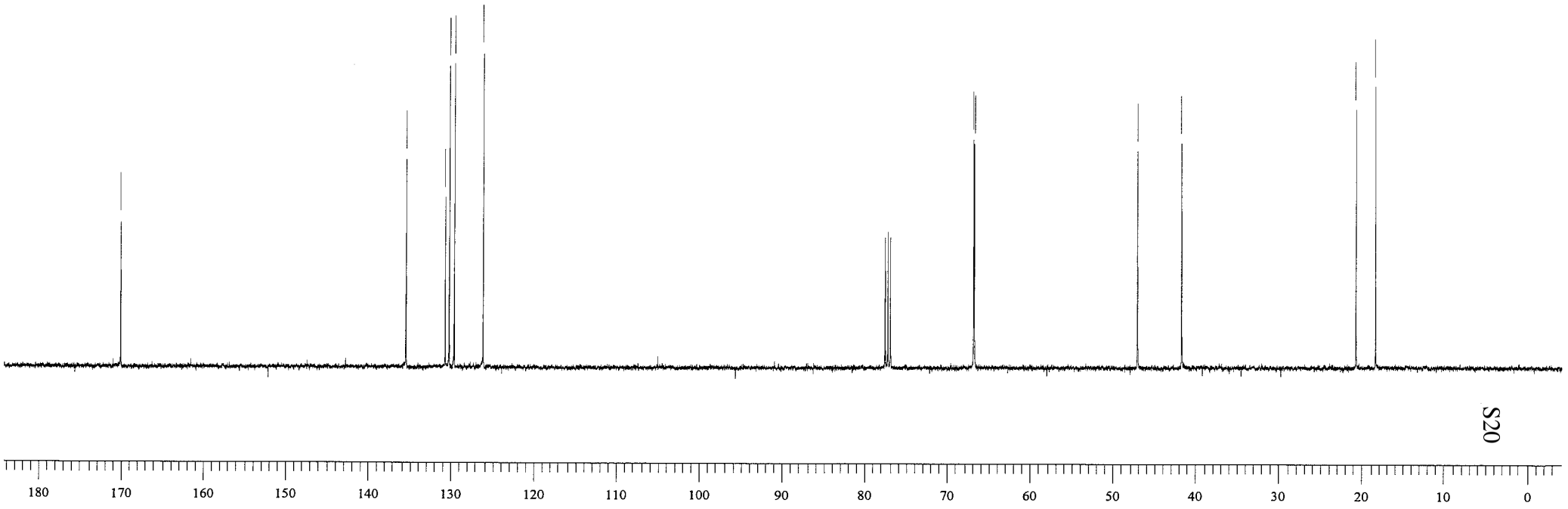

df 305 J

$CDCl_3$

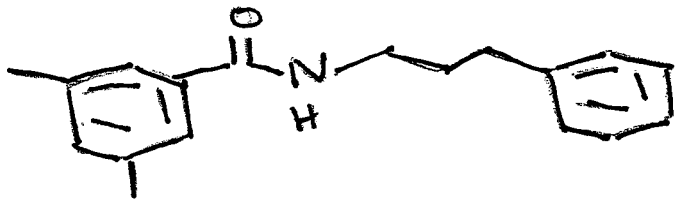

Table 3, Entry 3

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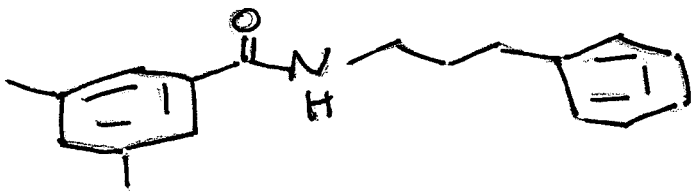

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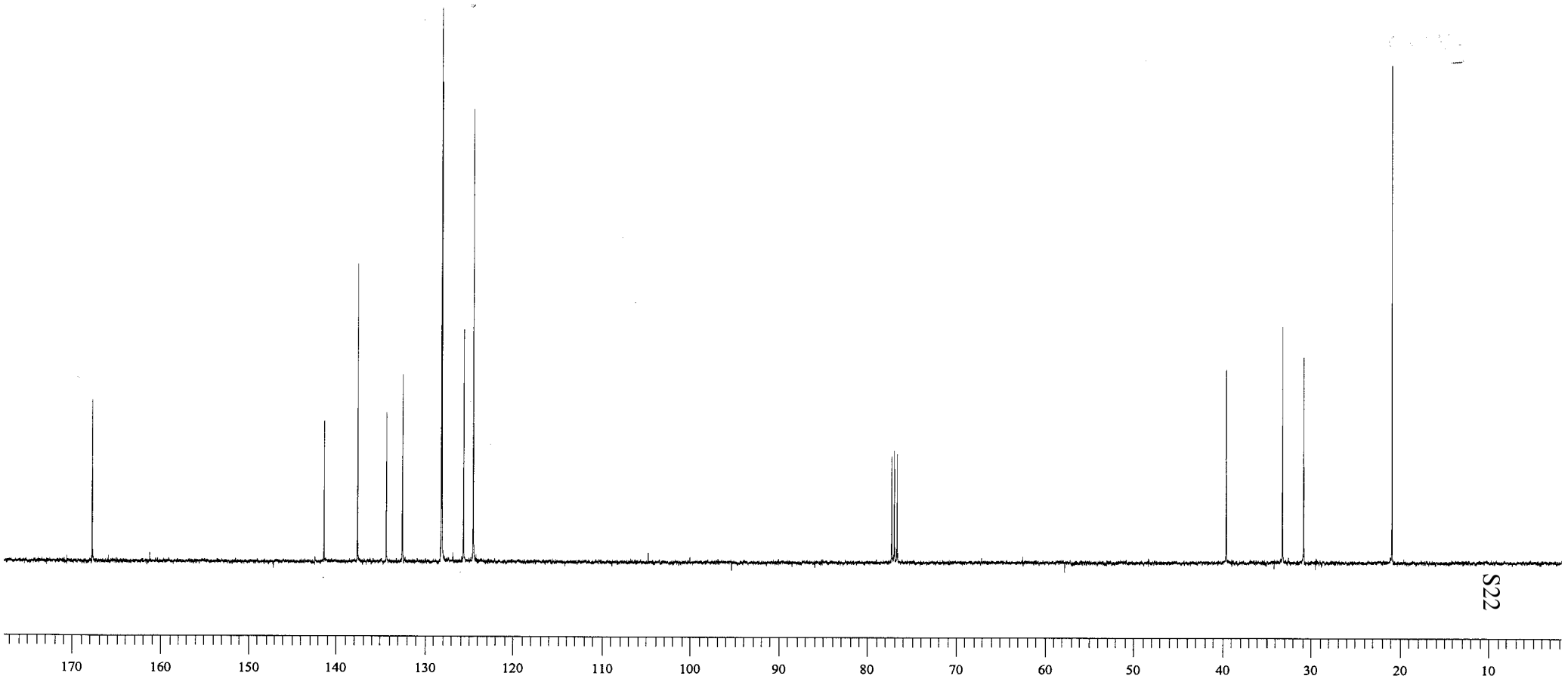

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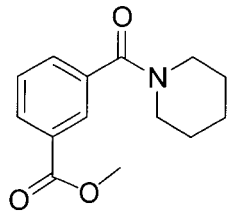

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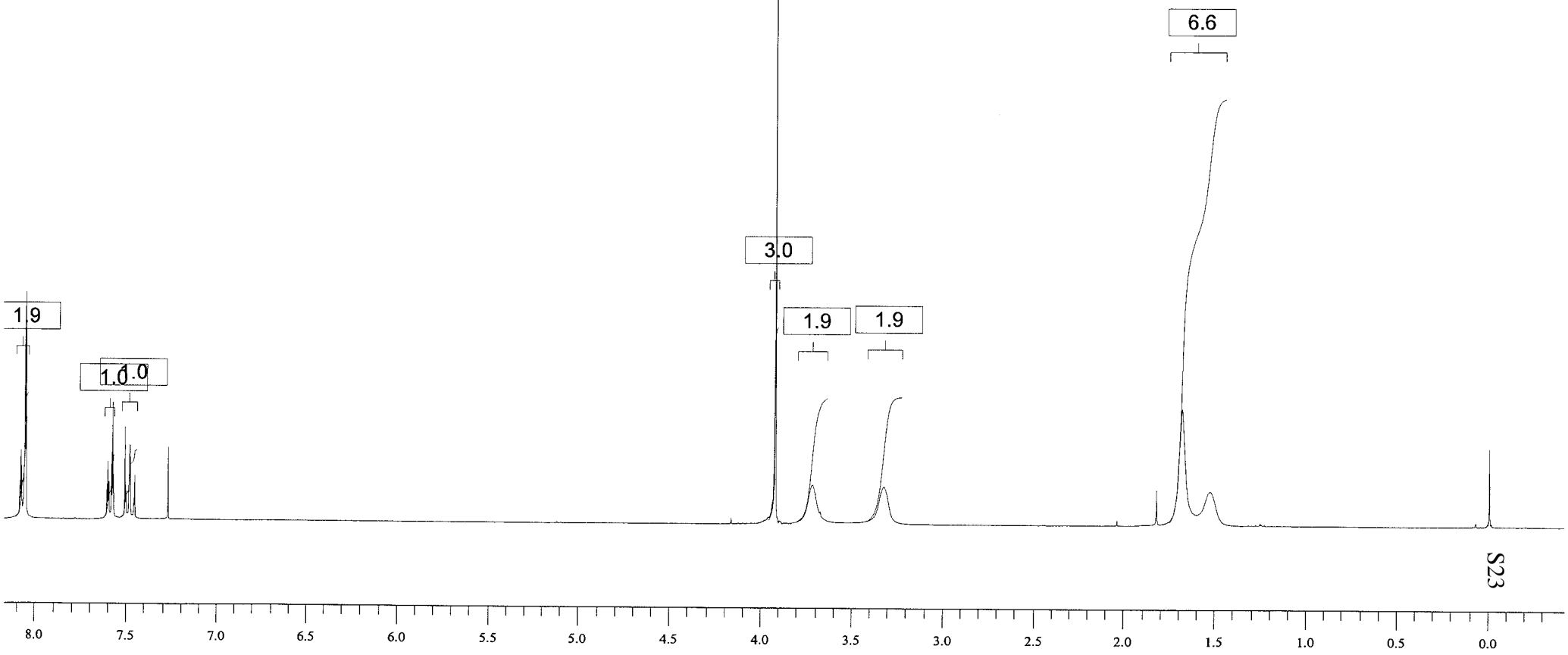

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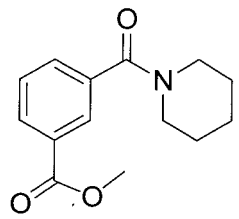

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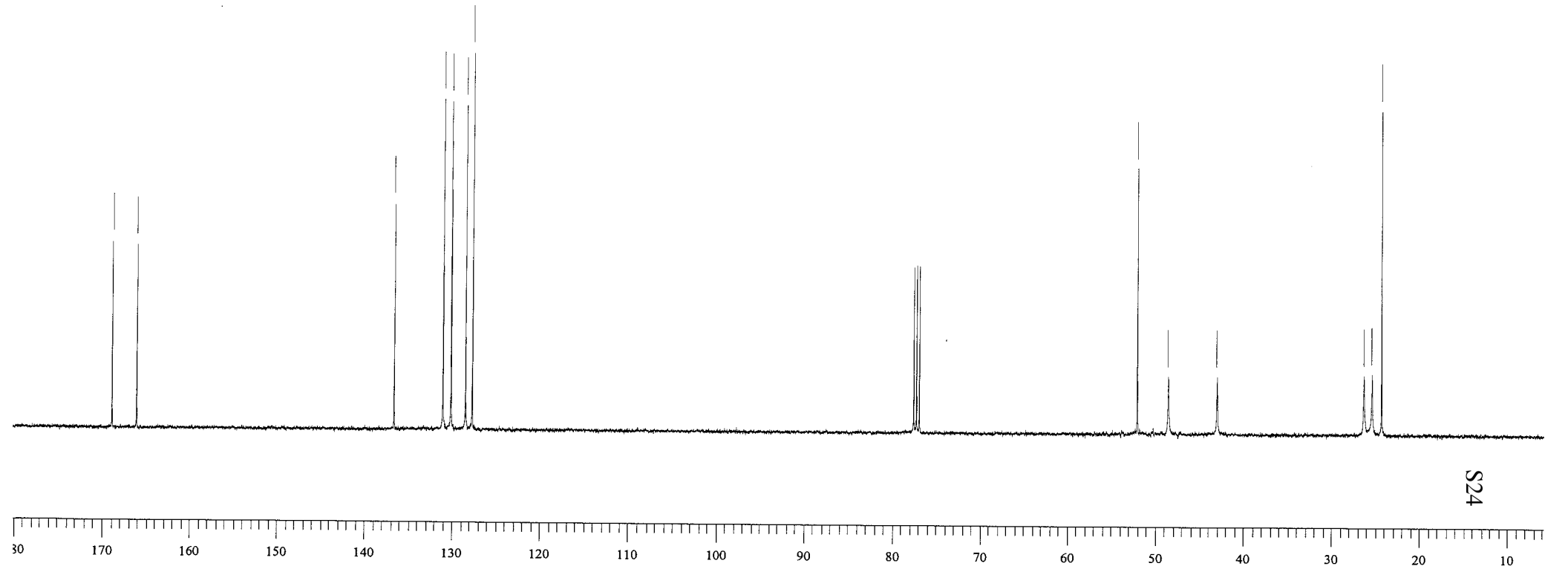
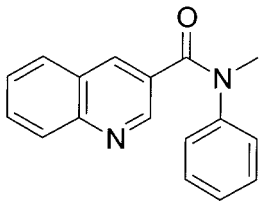


df 420 Quinoline-3-carboxylic acid methyl-phenyl-amide (400 MHz, CDCl3)



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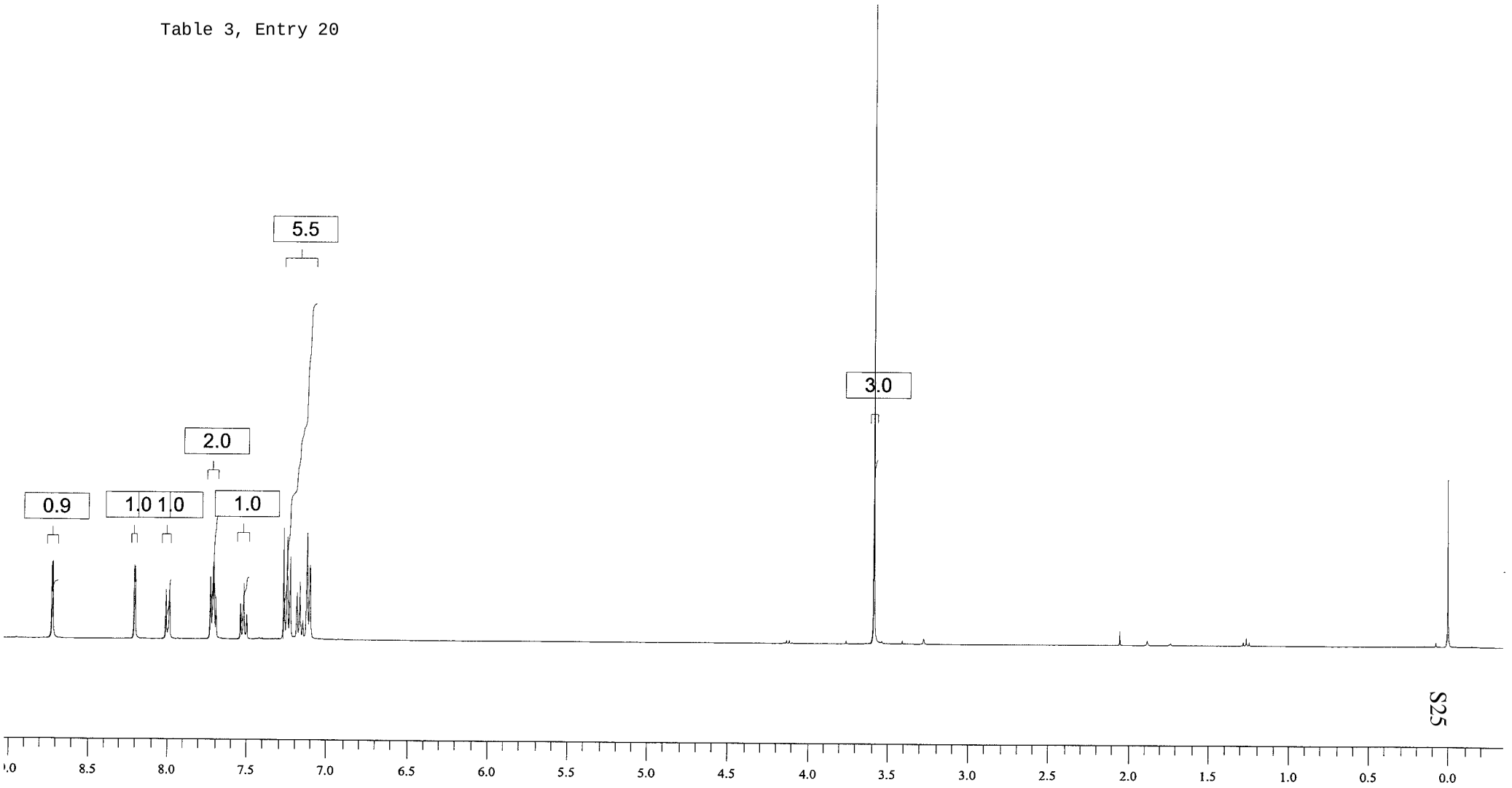

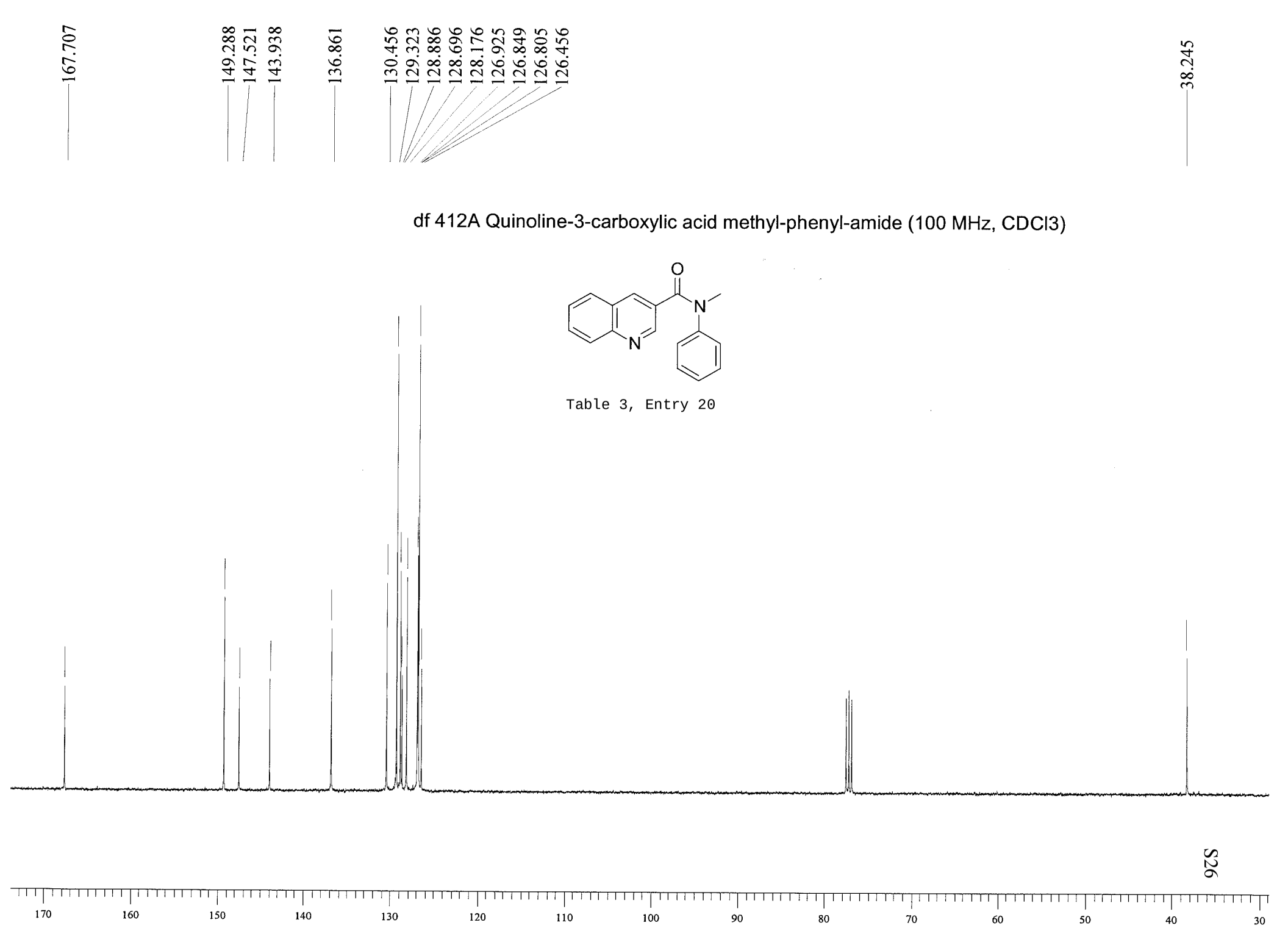
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128.176
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126.849
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126.456
38.245
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O
N
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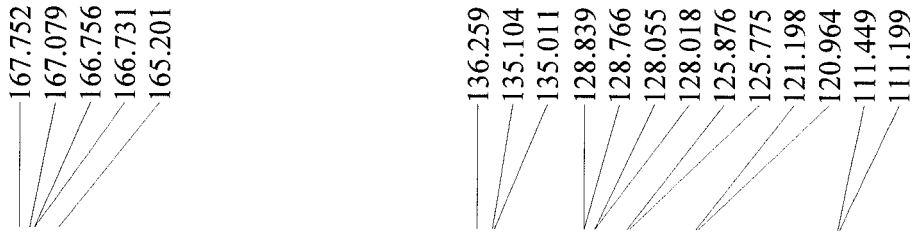

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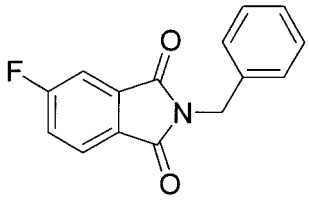

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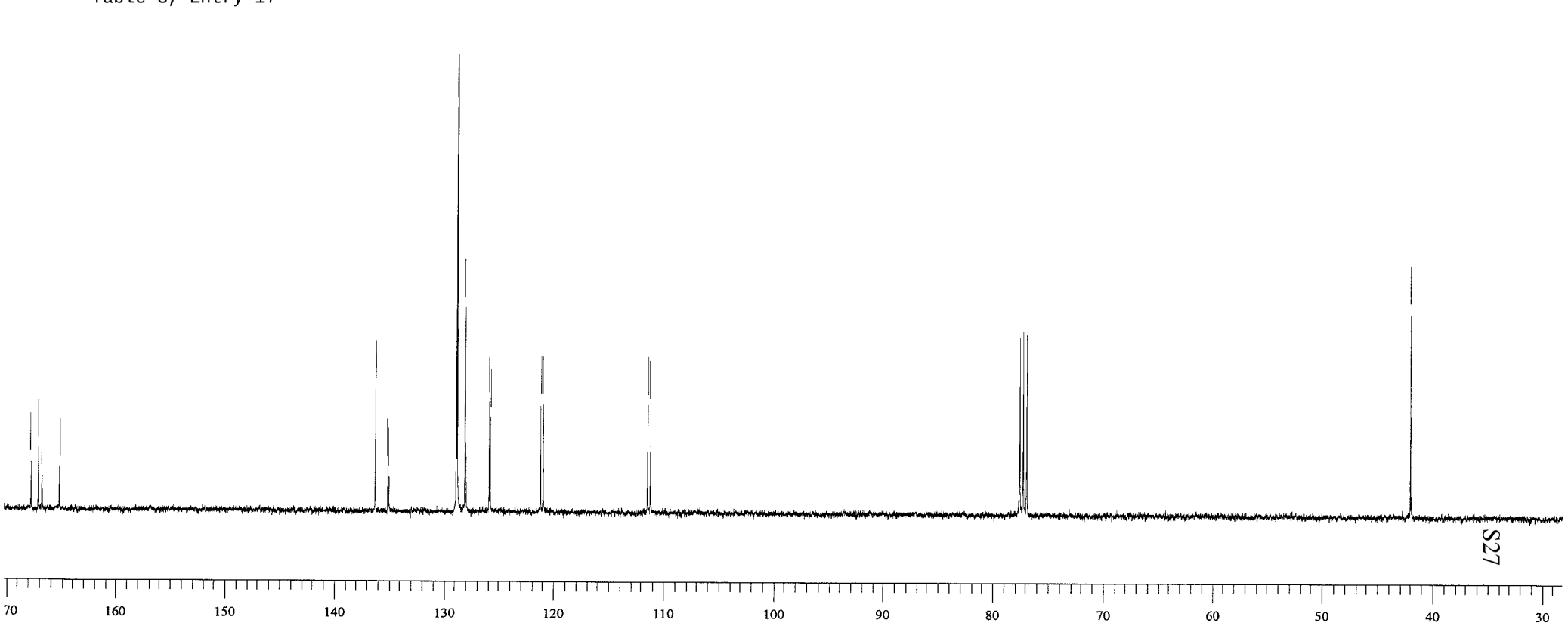

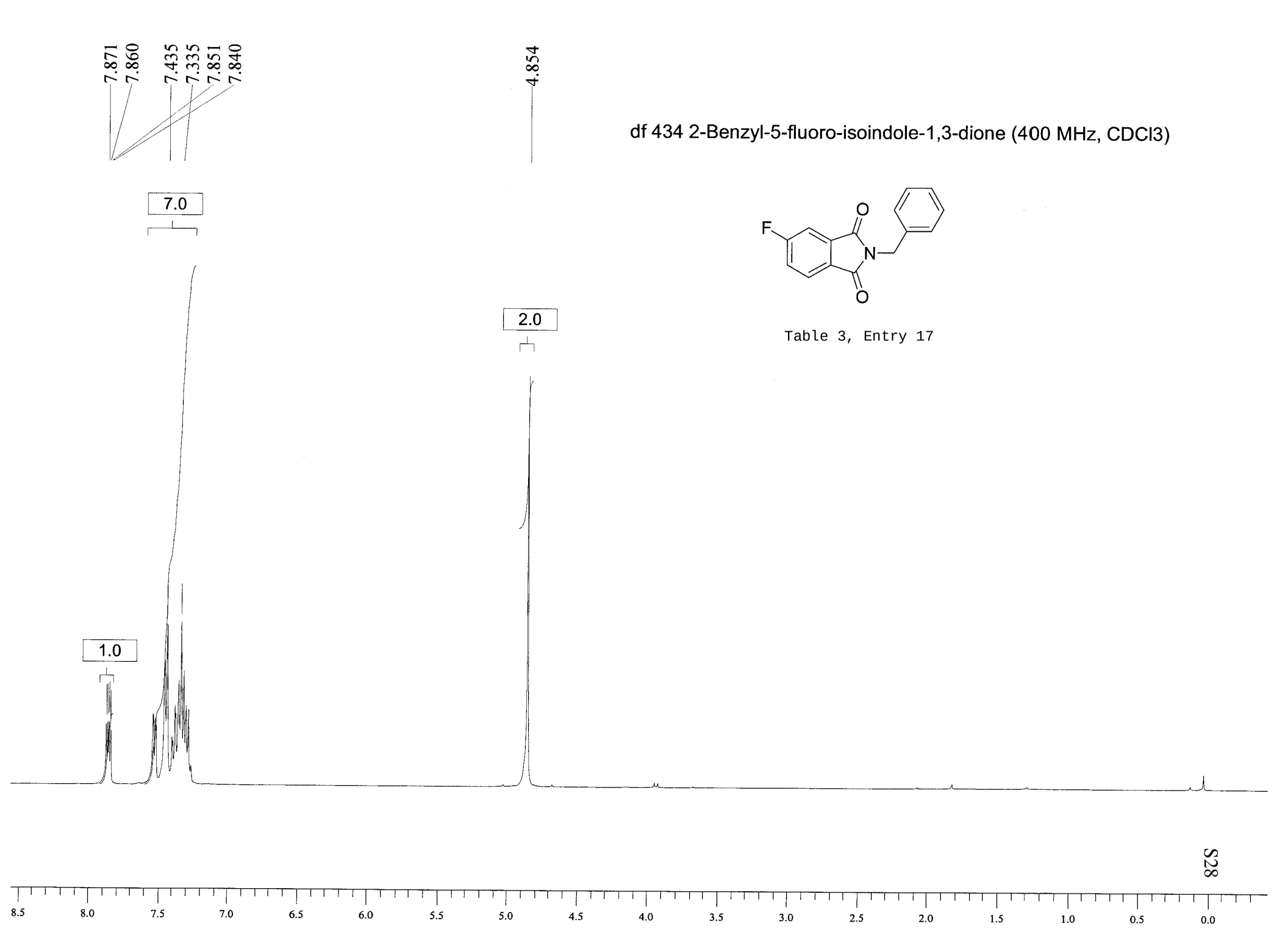
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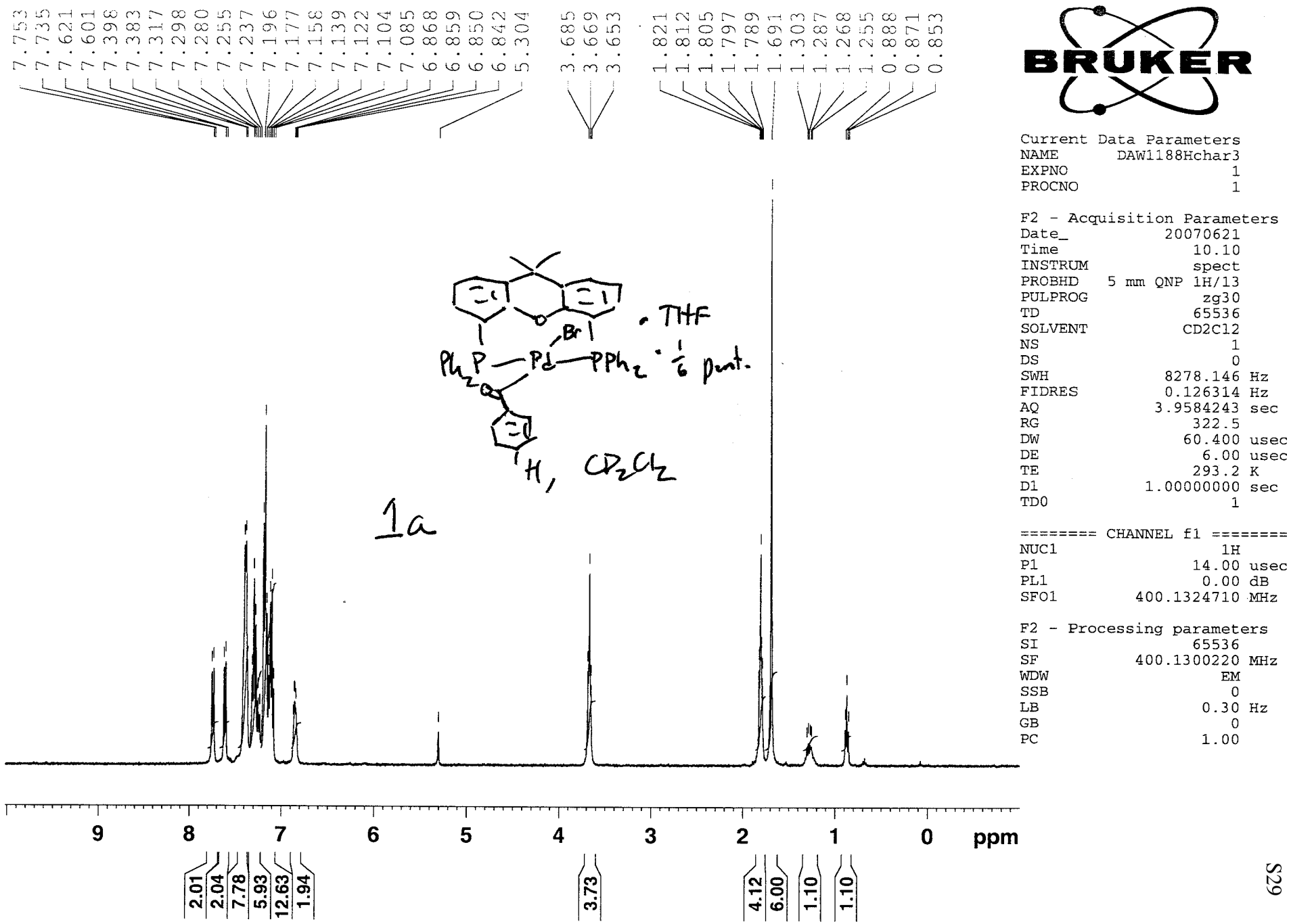

BRUKER

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D1              1.00000000 sec
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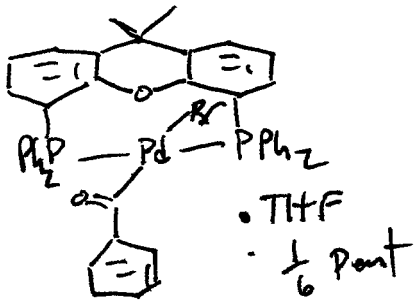

1a

31P

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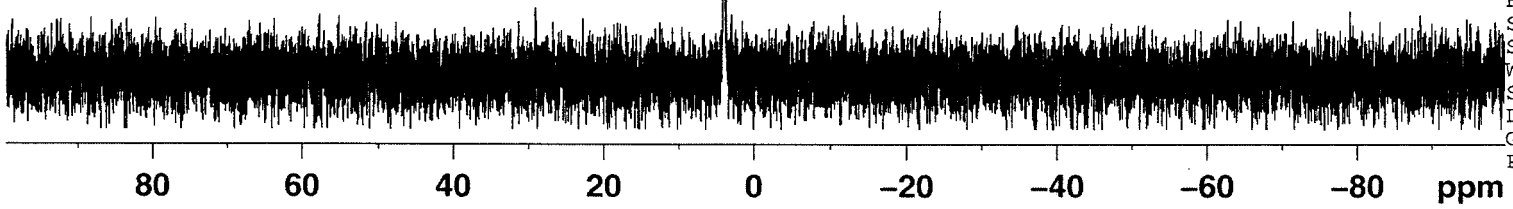

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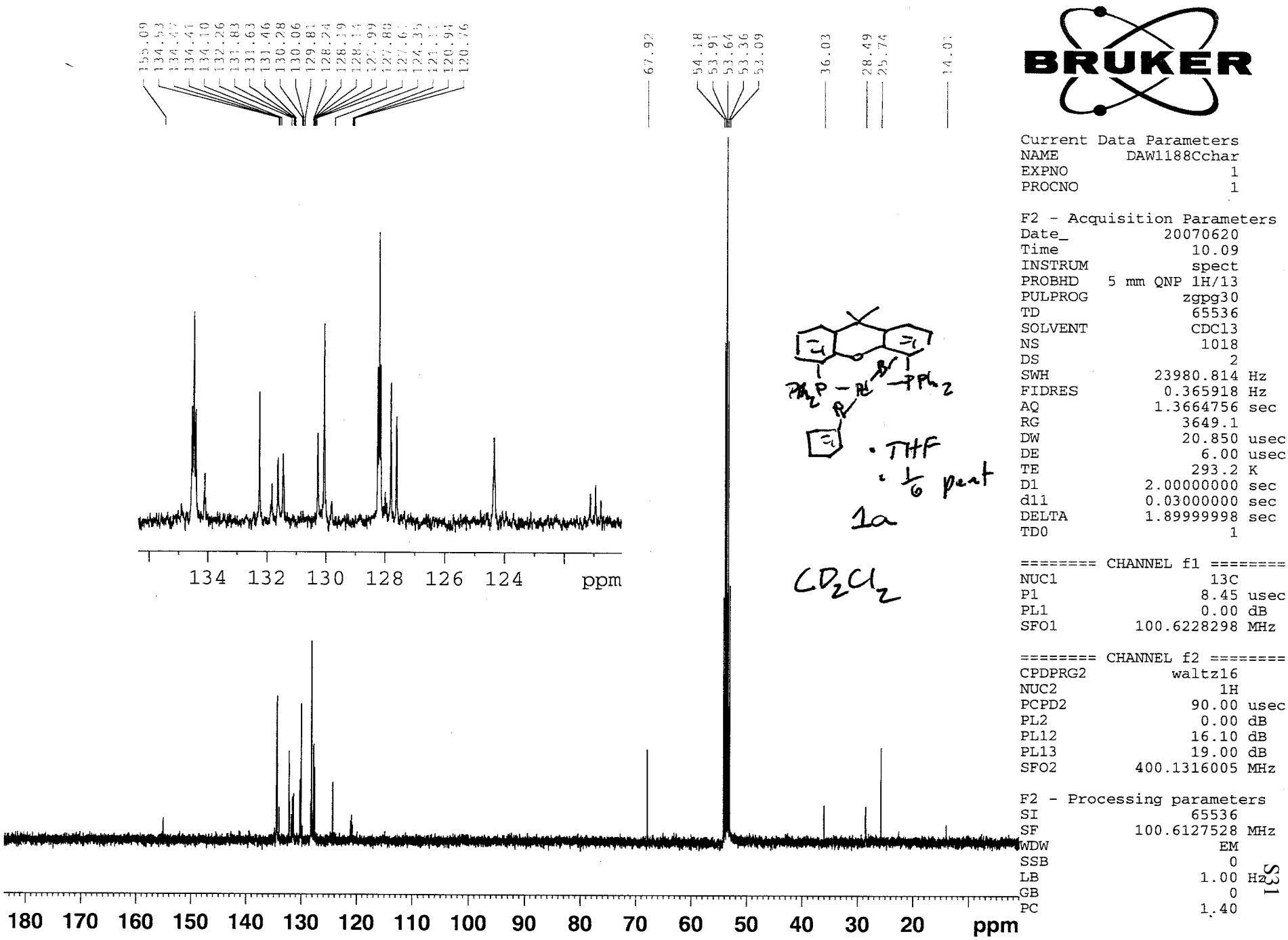
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BRUKER
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PL13 19.00 dB
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F2 - Processing parameters
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WDW EM
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GB 0
PC 1.40
• THF
• 1/6 part
1a
CD2Cl2